

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No. 076333/0148

In re patent application of

Joel S. Greenberger

Group Art Unit: 1633

Serial No. 09/075,532

Examiner: S. Chen

Filed: May 11, 1998

For: PROTECTION OF THE ESOPHAGUS FROM
IRRADIATION DAMAGE BY GENE THERAPY

DECLARATION UNDER 37 C.F.R. §1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

I, Dr. Chandra P. Belani declare that:

1. I am a citizen of the United States, residing at 208 Edelweiss Drive (P.O. Box 1056), Wexford, PA 15090-1056.
2. I graduated from Sawai Man Singh Medical College, Jaipur, India, and did my post graduate training and fellowship in hematology/oncology at the University of Maryland School of Medicine in Baltimore, MD. Following my fellowship I was on the faculty at the University of Maryland School of Medicine and then at University of Pittsburgh School of Medicine. I have expertise in the field of thoracic malignancies, especially lung and esophageal cancer.
3. I am employed presently as a Professor of Medicine at the University of Pittsburgh School of Medicine and co-director of the University of Pittsburgh Cancer Institute's Lung Cancer Center.
4. I have been engaged for over 10 years in the management of the complications of combination chemotherapy for lung cancer and esophagus cancer. One of

the most significant problems in treating lung cancer with active drugs, including carboplatin and Taxol, is the propensity of these drugs to interact with irradiation in the treatment of the primary tumor in the chest. Methods to protect the esophagus from radiation and/or chemotherapy damage are greatly needed.

5. I have followed with great interest the work of Dr. Joel Greenberger on the use of manganese superoxide dismutase (MnSOD) gene therapy for protection of the mouse esophagus from chemotherapy and radiation damage. I have been very impressed by the results achieved with this therapy in mice, as reported by Dr. Greenberger in *Radiation Oncology Investigations: Basic and Clinical Research*, and I have seen no comparable technique with chemical modifiers, locally protective pharmacologic agents, or other gene therapy techniques that can match these results. Based on the promise that this technique has shown in animal model and *in vitro* studies, I have been happy as Co-director of the Lung Cancer Center at the University of Pittsburgh Cancer Institute to support Dr. Greenberger in the design of translational methods to get this therapy into clinical trials at the Cancer Center.

6. I am particularly encouraged by the results Dr. Greenberger has achieved with plasmid liposomes in the mouse esophagitis model and organ explants, and I believe that a clinical trial in humans will be the only way to show that plasmid liposomes are effective in a clinical setting in providing protection from the adverse effects of chemotherapy and radiation therapy. In addition, other vectors such as adeno-associated virus, adenovirus, retrovirus, Lenti virus and herpes virus, may prove to be effective in Dr. Greenberger's method.

7. I believe that if the results with MnSOD in the human trials are positive then they can be extended to transgenes of other agents that neutralize or eliminate toxic species such as free radicals, superoxide anions and heavy metal cations, particularly gene products of other oxidant response gene families. Examples of such other agents include glutathione peroxidase, catalase, gamma-glutamyl transpeptidase, metallothioneine, and other agents that might block radiation-induced apoptosis, including BCL-XL, antisense BCL-2, and antisense BAX.

I hereby declare that all the statements made herein of my known knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful false statements are so made punishable by fine or imprisonment, or both, under Section 101 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

12/9/99
Date

CPB Belani
Chandra P. Belani, MD